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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/759,841	GRAHAM ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/29/06,2/21/07,10/31/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *66-69,72-76,79,80,82 and 115-162* is/are pending in the application.

4a) Of the above claim(s) *75,76,79,80,120,122,144 and 146* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-69,72-74,82,115-119,121,123-143,145,147-162* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/100,812.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :6/30/05,2/25/05,2/11/05,12/21/04,8/4/04,1/15/04,8/5/07.

DETAILED ACTION

Claims 66-69, 72-76, 79, 80, 82, and 115-162 are pending.

Election/Restrictions

Applicant's election with traverse of Group I and species SV40 late promoter in the reply filed on 10/31/06 is acknowledged. The traversal is on the ground(s) that the Patent Office has not established that undue burden would be required to search and examine both groups, the examiner has not alleged a credible use of the product in a materially different process, and the amendment to claims 66 and 67 indicate that the product is not suitable in prokaryotic cells. This is not found persuasive because the product can be used in plant cells or to make a dsRNA with concatamers, a PCR product, cloning product, a RNA hairpin, or ribozyme that is not required in the method of Group II and the search and examination for Group I requires a search of the prior art under 102 and 103 and examination under 112 first paragraph.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's election without traverse of species ssRNA target gene in the reply filed on 12/29/06 is acknowledged.

Claims 75, 76, 79, and 80 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/31/06.

DNA polymerase and viral coat protein in claims 116 and 140 and claims 120, 122, 144, 146 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a

nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/29/06.

Information Disclosure Statement

The examiner has considered the search reports and written opinion, but did not initial them on the PTO-1449 because the documents are not considered published documents.

The exhibits on the IDS filed on 3/5/07 as civil ligation actions have been considered, but the documents cited in the exhibits have not been considered for the reasons set forth in the previous office action.

Priority

It is not apparent if the oath incorrectly lists the foreign document as PP 2292. The number of the foreign document appears to be PP 2492. See document in parent application.

The foreign application PP2492 cited in the cross reference on page 1 of the specification is disclosed in an application data sheet but not the oath.

The foreign application PP2292 cited in the oath is not listed in the cross reference on page 1 of the specification.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/100,812, filed on 6/19/98. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one

or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 09/100,812, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

Instant claims 66-69, 72-74, 82, 115-119, 121, 123-143, 145, and 147-162 do not have written support under 112 first paragraph for a genus of. The specification of '812 contemplates: "at least about 20-30 nucleotides in length derived from a viral DNA polymerase, viral RNA polymerase, viral coat protein, or visually-detectable gene, more particularly an RNA polymerase gene derived from a virus selected from the list comprising BEV, Sinbis alphavirus, HIV-1, bovine herpes virus and HSV1 or a visually detectable gene which is involved in determining pigmentation, cell death or other external phenotype on a cell, tissue, organ, or organism, amongst others" and "the structural gene component of the synthetic gene comprises at least about 20-30 nucleotides in length derived from the BEV RNA-dependent RNA polymerase gene or the murine tyrosinase gene or the Escherichia coli lac repressor gene lacI or a complementary sequence thereto." See column 6, lines 25-40. It is not sufficient to

contemplate a genus of target gene or region thereof to support the present claimed invention directed to a genus of structural gene. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming a genus of structural genes that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of structural genes that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Instant claims 128, 129, 152, and 153 do not have written support under 112 first paragraph for the limitation 'no more than 2.0 kilobases' in claims 128 and 152 and the limitation 'no more than 0.5 kilobases (kb)' in claims 129 and 153. See MPEP § 2163.06.

Applicant cites several pages in the specification for support for all the amended and new claims, but does not specifically indicate where the limitation in the claims have support. The examiner had to search the entire specification for the limitations. It appears that the only support for the limitations is on page 17, lines 20-22. However, on page 17, the support is for no more than 0.5-2.0 kb, not no more than either 0.5kb or 2.0kb with no lower limit. Thus, it appears that the specification only provides support for no more than 0.5-2.0 kb not below 0.5kb. See In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 127, 128, 129, 151, 152, and 153 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New Matter:

There does not seem to be support for the limitation 'no more than 2.0 kilobases' in claims 128 and 152 and the limitation 'no more than 0.5 kilobases (kb)' in claims 129 and 153. See MPEP § 2163.06. Applicant cites several pages in the specification for support for all the amended and new claims, but does not specifically indicate where the limitation in the claims

have support. The examiner had to search the entire specification for the limitations. It appears that the only support for the limitations is on page 17, lines 20-22. However, on page 17, the support is for no more than 0.5-2.0 kb, not no more than either 0.5kb or 2.0kb with no lower limit. Thus, it appears that the specification only provides support for no more than 0.5-2.0 kb not below 0.5kb. See In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976).

There does not seem to be support for the limitation 'the stuffer comprises an intron' in claims 127 and 151. See MPEP § 2163.06. Applicant cites several pages in the specification for support for of the new claim, but does not specifically indicate where the limitation in claim 127 has support. The examiner had to search the entire specification for the limitations. It appears that the only support for the limitations is on pages 15-16. However, on page 15, line 30 to page 16, line 8 specifically recites: wherein the nucleic acid sequence comprises intron/exon splice junction sequences the stuffer fragment may serve as an intron sequence placed between the 3'-splice site of the structural gene nearer the 5'-end of the gene and the 5'- splice site of the next downstream unit thereof. Thus, it appears that the specification only provides support for using an intron as the stuffer between a sequence comprising intron/exon splice junction sequence. See In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976).

Claims 66-69, 72-74, 82, 115-119, 121, 123-143, 145, and 147-162 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are broadly drawn and read on a synthetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell. The broadest claims are not limited to any particular target genes from any particular organisms, reading on a large number of dsRNAs that are made that are substantially identical to at least any portion of any selected target gene from any source, that will function, as an dsRNA, to modulate gene expression. In view of the elected species, the claims read on a genus of target genes encoding RNA polymerase from a genus of ssRNA viruses.

However, the specification as filed does not provide an adequate written description of the vast genus of dsRNAs that are substantially identical to at least any portion of any selected target gene, that will function, commensurate with the breadth of what is claimed, as siRNAs to reduced duplex stability, to modulate (reduce or induce, for example) the expression of any target RNA molecule.

The specification as filed provides description or limiting definition of what is encompassed by substantial identity to a portion of a selected target gene or what it means to be substantially identical to a portion of a selected target gene. The specification as filed provides description or limiting definition of what is encompassed by a portion of a selected target gene. As discussed above under the priority section, the instant specification provides a general description of (pages 7-11) wherein it discloses that they are those dsRNAs that effective in achieving modulation or attenuation of gene expression. The specification discloses minimal examples of methods of making dsRNAs as claimed (page 25-39).

Therefore, in disclosing only broad and general guidance in regards to what is claimed, which is a method of making a dsRNA that is substantially identical to at least any portion of any

selected target gene, that will function, commensurate with the breadth of what is claimed, as dsRNAs to modulate (reduce or induce, for example) the expression of that selected target gene and only limited examples of the claimed dsRNAs, the specification does not provide a representative number of species of the method of making, as claimed, that would be sufficient to show possession of the vast genus of methods now claimed.

The specification does not provide the specific description that would be required to reasonably lead one of skill in the art to the instant invention or that would allow the skilled artisan to recognize that Applicant was in possession of the instant invention. The specification does not disclose how to make a representative number of species of the claimed genus with the desired biological function. The prior art does not supplement how to make a representative number of species of the claimed genus with the desired biological function (See Parrish et al. (Molecular Cell 6: 1077-1087, 2000, Perkel, The Scientist, pages 1-5, 2006, Shi TRENDS in Genetics 19: 9-12, 2003, and Vickers et al., The Journal of Biological Chemistry, 278:7108-7118, 2003). See Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996). Furthermore, the art of record as evidenced by Elbashir et al. 2001 (cited on a PTO 1449, 1/15/04) who provide a general outline for the construction of interfering RNAs (siRNAs) and point out that target recognition for interfering RNAs is highly sequence specific and that the nucleotide sequence at the target site and/or the accessibility of the target RNA structure may be responsible for variations in efficiency observed in their experiments with siRNA (pg. 6885, col. 2).

MPEP § 2163[R-2] I. states:

To satisfy the written description requirement, a patent specification must describe the

> claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., > Moba, B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003);< Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116.
>
> The fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., Vas-Cath, Inc., 935 F.2d at 1563-64, 19 USPQ2d at 1117.
>
> Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").
>
> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. > Enzo Biochem, 323 F.3d at 964, 63 USPQ2d at 1613.<

In the instant case, Applicant has not provided adequate written description of their invention because the specification does not convey, with reasonable clarity to those of skill in the art, as of the filing date sought, that applicant was in possession of the invention now claimed. Applicant has not shown how the invention was "ready for patenting" such as by the disclosure of a method as claimed, that made an dsRNA that is substantially identical to at least any portion of any selected target gene, that will function, commensurate with the breadth of what is claimed, as dsRNAs that is capable of delaying, suppressing, or otherwise reducing the expression of that selected target gene, for example.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 66, 67, 68, 69, 72, 73, 74, 82, 115, 117-119, 121, 123-125, 128, 130-139, 141-143, 145, 147, 148, 149, 152, and 154-162 are rejected under 35 U.S.C. 102(e) as being anticipated by Fire et al (US 6,506,559, cited on a PTO-1449). Fire teaches a vector comprising a construct comprising a promoter operably linked to a nucleotide sequence comprising dsRNA comprising a sense strand and an antisense strand of the target gene (columns 4 and 9). The dsRNA may be formed by a single self-complementary RNA strand or two complementary RNA strands (column 7). The construct comprises a regulatory region including polyadenylation (columns 8-9). The nucleotide sequence may be at least 25 or 50 bases (column 8). The vector can be introduced into a cancerous cell, including cancer cells find in humans (column 9-10). A viral vector or lipid mediated carrier transport can be used as the vector (column 9). The cell can comprise a target gene at risk from a pathogen including HIV or can be from several different types of animals (columns 4, 8, and 10). The construct can comprise a structural gene with an intron. In addition, the structural gene can comprise a 5' or 3' untranslated region (column 20). The structural gene can be less than 2.0 kilobases (table 1 and Figure 1). The structural gene can comprise one or more strands of the nucleotide sequence (column 4).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 68, 126, 138, and 150 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al (US 6,506,559, cited on a PTO-1449) taken with Ladner et al (US 5,198,346). Fire teaches a vector comprising a construct comprising a promoter operably linked to a

nucleotide sequence comprising dsRNA comprising a sense strand and an antisense strand of the target gene (columns 4 and 9). The dsRNA may be formed by a single self-complementary RNA strand or two complementary RNA strands (column 7). The construct comprises a regulatory region including polyadenylation (columns 8-9). The nucleotide sequence may be at least 25 or 50 bases (column 8). The vector can be introduced into a cancerous cell, including cancer cells find in humans (column 9-10). A viral vector or lipid mediated carrier transport can be used as the vector (column 9). The cell can comprise a target gene at risk from a pathogen including HIV or can be from several different types of animals (columns 4, 8, and 10). The target gene can be an endogenous from in a human cell (columns 4 and 10-11). The construct can comprise a structural gene with an intron. In addition, the structural gene can comprise a 5' or 3' untranslated region (column 20). The structural gene can be less than 2.0 kilobases (table 1 and Figure 1). The structural gene can comprise one or more strands of the nucleotide sequence (column 4). However, Fire does not specifically teach separating a construct comprising the structural gene sequences with a stuffer sequence of nucleotides 10-50 nucleotides in length.

However, at the time the invention was made, Lander teaches using a stuffer fragment having above about 10 nucleotides to introduce a stop codon or a unique restriction site (column 136 and Table 704). Lander teaches using a transcription termination sequence and a promoter to regulate transcription of the gene (column 136).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with Ladner, namely to produce a construct comprising a structural gene with a stuffer sequence. One of ordinary skill in the art

would have been motivated to combine the teaching to introduce a termination site after the sense strand or a unique restriction sequence for cloning purposes.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with Ladner, namely to produce an isolated animal cell comprising a construct comprising a structural gene with a stuffer sequence. One of ordinary skill in the art would have been motivated to combine the teaching for studying inhibition in animal cells in vitro using the construct with or without a stuffer sequence.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with Ladner, namely to produce a construct comprising a structural gene with a stuffer sequence, wherein the structural gene is operably linked to a promoter and termination sequence. One of ordinary skill in the art would have been motivated to combine the teaching for signaling termination of the transcription. On pages 22-23 of the instant specification, the applicant teaches that any promoter and termination sequence may be used.

In view of the teaching of Fire (columns 8-9), one of ordinary skill in the art would have had a reasonable expectation of success of producing the dsRNA construct.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 68, 127, 138, and 151 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al (US 6,506,559, cited on a PTO-1449) taken with German et al. (US 6,225,290).

Fire teaches a vector comprising a construct comprising a promoter operably linked to a nucleotide sequence comprising a sense strand and an antisense strand of the target gene (columns 4 and 9). The construct comprises a regulatory region including polyadenylation (columns 8-9). The nucleotide sequence may be at least 25 or 50 bases (column 8). The vector can be introduced into a cancerous cell, including cancer cells find in humans (column 9-10). The target gene can be an endogenous from in a human cell (columns 4 and 10-11). The structural gene can comprise one or more strands of the nucleotide sequence (column 4). However, Fire does not specifically teach separating a construct comprising the structural gene sequences with a stuffer sequence comprising an intron, wherein the stuffer sequence spatially separates the gene sequences. In view of the breadth of the term "two copies are spatially separated by a s stuffer fragment which comprises an intron" the term reads on the stuffer being located between the two sequences including the stuffer being located before the first structural gene in a circular plasmid.

However, at the time the invention was made, German teaches that including one or more introns in a construct can increase the level of expression of a DNA of interest in the construct (columns 7-8). German teaches inserting the intron into the construct at a 5' position to the DNA of interest (Column 8).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with German, namely to produce an isolated animal cell comprising a construct comprising a structural gene with a stuffer sequence comprising an intron. One of ordinary skill in the art would have been motivated to

combine the teaching to improve the efficient of expression of the structural genes by placing an intron 5' to each structural gene.

In view of the teaching of Fire (columns 8-9), one of ordinary skill in the art would have had a reasonable expectation of success of producing the dsRNA construct.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 68, 116, 139, 140are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al (US 6,506,559, cited on a PTO-1449) taken with Cowsert et al. (US 5,580,767). Fire teaches a vector comprising a construct comprising a promoter operably linked to a nucleotide sequence comprising a sense strand and an antisense strand of the target gene (columns 4 and 9). The construct comprises a regulatory region including polyadenylation (columns 8-9). The nucleotide sequence may be at least 25 or 50 bases (column 8). The vector can be introduced into a cancerous cell, including cancer cells find in humans (column 9-10). The target gene can be an endogenous from in a human cell (columns 4 and 10-11). The structural gene can comprise one or more strands of the nucleotide sequence (column 4). However, Fire does not specifically teach targeting RNA polymerase of a viral gene.

However, at the time the invention was made, Cowsert teaches antisense for inhibiting RNA polymerase (column 3).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with Cowsert, namely to produce an isolated animal cell comprising a construct comprising a structural gene encoding RNA

polymerase of a virus. One of ordinary skill in the art would have been motivated to combine the teaching to improve the efficiency of inhibiting the virus.

In view of the teaching of Fire (columns 8-9) and Cowsert (column 3), one of ordinary skill in the art would have had a reasonable expectation of success of producing the animal cell comprising the dsRNA construct.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 68, 129, 139, and 153 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al (US 6,506,559, cited on a PTO-1449) taken with Gengenbach (US 6,069,298). Fire teaches a vector comprising a construct comprising a promoter operably linked to a nucleotide sequence comprising a sense strand and an antisense strand of the target gene (columns 4 and 9). The construct comprises a regulatory region including polyadenylation (columns 8-9). The nucleotide sequence may be at least 25 or 50 bases (column 8). The vector can be introduced into a cancerous cell, including cancer cells find in humans (column 9-10). The target gene can be an endogenous from in a human cell (columns 4 and 10-11). The structural gene can comprise one or more strands of the nucleotide sequence (column 4). However, Fire does not specifically teach the structural gene is no more than 0.5 kilobases (kb).

However, at the time the invention was made, Gengenbach teaches antisense to an about 0.5 kb region of the maize ACCase cDNA that has high homology to the chicken ACCase gene (column 37).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with Gengenbach, namely to produce an isolated animal cell comprising a construct comprising structural gene sequences no more than 0.5 kilobases. One of ordinary skill in the art would have been motivated to combine the teaching to improve the efficiency of inhibiting the ACCase gene.

In view of the teaching of Fire (columns 8-9), one of ordinary skill in the art would have had a reasonable expectation of success of producing the animal cell comprising the dsRNA construct.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 66, 67, 68, 69, 72-74, 82, 123-138, and 147-162 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 11-15, and 19-21 of Patent No. 6,573,099. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims are directed to a dsRNA construct.

Claims 66, 67, 68, 69, 72-74, 82, 123-138, and 147-162 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 56, 59, 60, 62, 63, 65-67, 77-101, and 107 of copending Application No. 09/646,807. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims read on a dsRNA construct for reducing expression of a target gene in an animal cell.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 66, 67, 68, 69, 72-74, 82, 123-138, and 147-162 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 34, 66, 78, 79, of copending Application No. 10/346,853. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims read on a dsRNA construct for reducing expression of a target gene in an animal cell.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 66, 67, 68, 69, 72-74, 82, 123-138, and 147-162 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 46, 47, 59-61, 66-70, and 74-80 of copending Application No. 11/180,928. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims read on a dsRNA construct for reducing expression of a target gene in an animal cell.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

NOTE: There at least five other co-pending applications that might have claims embracing the subject matter of the claimed invention, if Applicants are aware of any pending applications or patents containing claims that read on the claimed invention, which are not listed above, Applicants' are reminded of their duty to disclose these applications or patents. See 37 CFR 1.56.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 6:30 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz, SPE – Art Unit 1635, can be reached at (571) 272-0763.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Brian Whiteman